Please add the following new claims.

20. (NEW) The nucleic acid molecule of claim 11, wherein said nucleic acid molecule is fused to a nucleic acid molecule encoding a second protein.

21. (NEW) The nucleic acid molecule of claim 20, wherein said second protein is selected from the group consisting of hemagglutinin, GST, maltose binding-protein, or a fragment of any one of said second polypeptides.

C3 22. (NEW) The nucleic acid probe of claim 1, wherein said probe comprises a nucleotide sequence that encodes a polypeptide comprising at least 100 contiguous amino acids of SEQ ID NO: 1.

23. (NEW) The nucleic acid molecule of claim 20, wherein said nucleic acid molecule encodes a FRS2 polypeptide having the full length amino acid sequence set forth in SEQ ID NO: 1.

REMARKS

Status of the Claims

By this amendment, claims 4 and 11 are amended and claims 20-23 are added. Upon entry of this Amendment, claims 2, 4-6, 11-13 and 20-23 will be pending in the application.

Exemplary support for the amendments to claim 4 is found in the specification on page 12, line 11, through page 13, line 8. Exemplary support for the amendments to claim 11(c) is found throughout the specification. See, for example, page 5, lines 20-27 and page 10, lines 14-28. Exemplary support for the amendments to claim 11(d) is found in the specification on page 24, lines 15-19. Exemplary support for claims 20 and 21 is found in originally filed claim 19, which has already been examined by the Examiner. Additional exemplary support is found in originally filed claims 17 and 18, as well as in the specification on page 36, lines 7-23 and page 40, lines 14-25. Exemplary support for claim 22 is found in the specification on page 12, line 18. Exemplary support for claim 23 is found on page 24, lines 10-12.

Issues Under Priority

The Examiner asserts that the first page of the specification should be amended to recite the following:

> "This application is a divisional of U.S. Serial No. 08/980,523, filed December 1, 1997, now U.S. Patent No. 6,310,181, which is incorporated by reference in its entirety (including any drawings), and claims priority to U.S. Provisional Application No. 60/032,093, filed December 12, 1996."

Applicants request the Examiner to amend the specification by informal Examiner's amendment at the time of allowance.

Claim Objections

The Examiner objects to claims 1, 2, 4-6 and 11-13 because the first time the term "FRS2 polypeptide" appears in the claims, it should be written out in full, followed by the abbreviation in parenthesis. Applicants have amended claim 11(a) to recite "Fibroblast Growth Factor Receptor Protein Kinase Substrate 2 (FRS2)", as suggested by the Examiner.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

A. Claims 2, 4-6 and 11-13 are rejected by the Examiner under 35 U.S.C. § 112, second paragraph as being allegedly indefinite. The examiner asserts that while the specification recites a number of preferred structural or functional activities for the FRS2 polypeptide, it is unclear which of these characteristics are necessary limitations of the polypeptide encoded by the claimed nucleic acid. Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants disagree with the Examiner's assertion. However, in order to expedite prosecution, Applicants have amended claim 11(c) to recite that the FRS2 polypeptide has FRS2 activity. With respect to claim 4, applicants assert that the structural information provided in claim 4 is sufficient to render claim 4 definite to a person of ordinary skill in the art. Claim 4, as amended, is directed to a nucleic acid probe comprising a nucleotide

sequence that encodes a polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1.

B. Claim 11 is rejected by the Examiner as being under 35 U.S.C. § 112, second paragraph as being allegedly indefinite. Applicants have amended claim 11 as suggested by the Examiner. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

A. Claims 2, 4-6 and 11-13 are rejected by the Examiner under 35 U.S.C. § 112, first paragraph for lack of written description. Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that claim 4 is drawn to "structural limitations" of the "nucleic acid target molecule" and not the claimed nucleic acid probe. Applicants have amended claim 4 to recite "[a] nucleic acid probe comprising a nucleotide sequence that encodes a polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1." Therefore, in amended claim 4, the structural limitations apply to the nucleic acid probe.

The Examiner also asserts that claim 11 continues to encompass any possible nucleic acid which encodes any FRS2 polypeptide. Applicants have amended claim 11(d) to recite "encodes a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one, but not all, of the following segments of amino acid residues: 1-10, 11-152, or 153-508." Applicants note that in claims 7 and 8 of the parent application, now U.S. Patent No. 6,310,181, use similar claim language.

B. Claims 2, 4-6 and 11-13 are rejected by the Examiner under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. Applicants respectfully request reconsideration and withdrawal of the rejection.

With respect to claim 4, the Examiner asserts that a person of ordinary skill in the art would be required to construct the entire remainder of the molecule necessary for providing

the recited function, since there is allegedly no teaching in the specification that only 10 amino acids of the FRS2 polypeptide are sufficient for the recited function. Applicants respectfully disagree.

Nucleic acid probes are described in the specification on page 12, line 11, through page 13, line 8. Briefly, a nucleic acid probe is complementary to and can bind to a nucleic acid sequence encoding an amino acid sequence that is similar to the amino acid sequence set forth in SEQ ID NO: 1. Therefore, those of ordinary skill in the art know that nucleic acid probes can be use to detect the present or absence of nucleic acid molecules in various applications, such as diagnostic methods. A nucleic acid molecule encoding 10 amino acids comprises 30 nucleotides. A person of ordinary skill in the art would know that a nucleic acid probe comprising 30 nucleotides is of a sufficient size for performing the function of a nucleic acid probe.

The Examiner also asserts that the previous amendments to claim 4 were drawn to the "structural" limitations of the "nucleic acid target molecule", not to the claimed nucleic acid probe. As discussed above, Applicants have amended claim 4 to recite "[a] nucleic acid probe comprising a nucleotide sequence that encodes a polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1."

Turning to claim 11, the Examiner asserts that part (d) continues to encompass any possible nucleic acid which encodes any FRS2 polypeptide. As discussed above, Applicants have amended claim 11(d) to recite "encodes a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one, but not all, of the following segments of amino acid residues: 1-10, 11-152, or 153-508."

Finally, on page 8 of the Office Action the Examiner states that Applicants have not taught how to use a nucleic acid that encodes an FRS2 polypeptide. As discussed above, the specification provides sufficient disclosure to enable a person of ordinary skill in the art to make and use the nucleic acid molecule of the present invention. See, for example, page 4, lines 7-28 and page 12, line 11, through page 12, line 8.

Claim Rejections - 35 U.S.C. § 102

Claims 4 and 11 are rejected by the Examiner under 35 U.S.C. § 102 as being anticipated by Ottillie et al. The Examiner asserts that the previous amendments to claim 4 were drawn to the structural limitations of the "nucleic acid target molecule" and not the claimed nucleic acid probe. The Examiner further asserts that the previous amendments to claim 11 (d) produced a claim that encompasses any possible nucleic acid which encodes any FRS2 polypeptide. Applicant(s) respectfully request(s) reconsideration and withdrawal of the rejection.

Claim 4 is not anticipated by Ottillie et al. Claim 4, as amended, states that the nucleic acid probe comprises a nucleotide sequence that encodes a polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1. The first 6 amino acids of the sequence of Ottilie et al. and SEQ ID NO: 1 share sequence homology. However, the rest of the amino acids in the two sequences share almost no homology. Applicants attempted to perform a Blast alignment of SEQ ID NO: 1 and the sequence of Ottilie et al., however; there were no regions of homology identified. Therefore, the largest region of contiguous amino acids shared between SEQ ID NO: 1 and the sequence of Ottilie et al. is 6 amino acids.

Claim 11 is also not anticipated by Ottillie et al. The sequence of Ottilie et al. does not satisfy any of the requirements of claim 11. In particular, since the Blast alignment discussed in Applicants' previous amendment dated October 23, 2003 did not identify any regions of sequence homology, the sequence of Ottilie et al. does not share 90 % sequence identity to the amino acid sequence of SEQ ID NO: 1, as stated in part (c) of claim 11. Furthermore, applicants have amended claim 11(d) to recite "encodes a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one, but not all, of the following segments of amino acid residues: 1-10, 11-152, or 153-508." Therefore, claim 11(d) requires that at least one of the recited segments of amino acid residues is present.

Claim Rejections - 35 U.S.C. § 103

Claims 2, 4-6 and 11-13 are rejected by the Examiner under 35 U.S.C. § 103 as being obvious over Wang et al. The Examiner asserts that based on many of the shared characteristics of the SLP protein taught by Wang et al. and that of the FRS2 protein of the instant application, the nucleic acids that encode a SLP protein are thought to be encompassed by nucleic acids that encode a FRS2 polypeptide. Applicants respectfully request reconsideration and withdrawal of the rejection.

As discussed above, Applicants have amended claim 4 to recite "[a] nucleic acid probe comprising a nucleotide sequence that encodes a polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1." Applicants have also amended claim 11(d) to recite "encodes a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one, but not all, of the following segments of amino acid residues: 1-10, 11-152, or 153-508." Therefore, the structural limitations of claim 4 apply to the nucleic acid probe. Additionally, the amendments to claim 11 (d) require that at least one of the recited segments of amino acid residues is present.

Furthermore, as discussed in Applicants previous amendment, Wang et al. fails to disclose any sequences for the SNT-like proteins discussed in the paper (the paper says "SLP" is a SNT-like protein). It is the Examiner's burden to provide evidence to support that the claimed sequence shares sequence identity or homology with the prior art sequence. Absent any evidence from the Examiner as to whether the protein of Wang et al. has any sequence identity or homology with the amino acid sequence of SEQ ID NO: 1, Applicants maintain that the claimed invention is not obvious over Wang et al. Attached herewith as Exhibit A, Applicants provide a copy of Xu et al. (1998) *JBC* **273** 17987-17990, which was published after the priority date of the present invention. The 1998 Xu et al. article and the cited Wang et al. article both list Hong Xu and Mitchell Goldfarb as authors. Sequences for "SNT" proteins are provided in Xu et al. (1998) article; however, the article provides no indication that the disclosed sequences are those of the proteins described in the cited Wang

et al. reference. Indeed, Wang et al. notes that "SLP" is an "SNT-like" protein, but Xu et al. 1998 provides sequences for "SNT" proteins. Applicants have been provided with no evidence supporting the notion that the claimed sequence shares sequence identity or homology with the prior art sequence.

CONCLUSION

As the above-presented amendments and remarks address and overcome all of the rejections presented by the Examiner, withdrawal of the rejections and allowance of the claims are respectfully requested.

If the Examiner has any questions concerning this application, he or she is requested to contact the undersigned.

Respectfully submitted,

Date 4/24/03

By _____

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109
Telephone: (202) 672-5475
Facsimile: (202) 672-5399

Beth A. Burrous
Attorney for Applicants
Registration No. 35,087

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

4. (Amended) A nucleic acid probe [for the detection of a nucleic acid molecule in a sample, wherein said nucleic acid molecule] comprising a nucleotide sequence that encodes a [FRS2] polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 1.

11. (Amended) An isolated, enriched, or purified nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes a Fibroblast Growth Factor Receptor Protein Kinase Substrate 2 (FRS2) polypeptide having the full length amino acid sequence set forth in SEQ ID NO: 1;

(b) is the complement of the nucleic acid sequence of (a);

(c) encodes a FRS2 polypeptide having at least 90% sequence identity to the amino acid sequence set forth in SEQ ID NO: 1 and having FRS2 activity;

(d) encodes a FRS2 polypeptide having the full length amino acid sequence of the sequence set forth in SEQ ID NO: 1 except that it lacks at least one, [or more] but not all, of the following segments of amino acid residues: 1-10, 11-152, or 153-508;

(e) is the complement of the nucleic acid sequence of (d);

(f) [is] encodes a polypeptide having the amino acid sequence set forth in SEQ ID NO: 1 from amino acid residues 1-10, 11-152, or 153-508;

(g) is the complement of the nucleic acid sequence of (f);

(h) encodes a polypeptide having the full length amino acid sequence set forth in SEQ ID NO: 1 except that it lacks one or more of the domains selected from the group consisting of a myristylation region, a phosphotyrosine binding region, and a C-terminal region;

(i) is the complement of the nucleic acid sequence of (h);

(j) encodes a polypeptide as set forth in (a), (d), or (f) containing one or both of the following mutations: tyrosine 349 to phenylalanine or tyrosine 392 to phenylalanine; or

(k) the complement of the nucleic acid sequence of (j).